AMENDMENTS TO THE SPECIFICATION

On page 1, before the heading "FIELD OF THE INVENTION" please add the following paragraph:

-- This application is the National Stage of International Application No. PCT/EP2003/08725, filed on August 7, 2003. --

Please replace the paragraph beginning at line 20 on page 5 of the specification with the following amended paragraph:

-- The mature amino acid sequence of human EPO contains 166 amino acid residues and depicted in single-letter code comprises the following sequence:
APPRLICDSRVLERYLLEAKEAENITTGCAEHCSLNENITVPDTKVNFYAWKRMEVGQQAV
EVWQGLALLSEAVLRGQALLVNSSQPWEPLQLHVDKAVSGLRSLTTLLRALGAQKEAISPP
DAASAAPLRTITADTFRKLFRVYSNFLRGKLKLYTGEACRTGDR (SEQ ID NO: 1). --

Please replace the paragraph beginning at line 23 on page 8 of the specification with the following amended paragraph:

-- an accordingly specified molecule wherein alteration is conducted at one or more residues from the string of contiguous residues defined herein as epitope regions and comprising one of the sequences
(a) RVLERYLLEAKEAENITTGCAEHCSLNENITVP (SEQ ID NO: 2; residues 10-42 of SEQ ID NO: 1),
(b) RGQALLVNSSQPWEPLQLHVDKAVSGLRSLTTL (SEQ ID NO: 3; residues 76-108 of SEQ ID NO: 1), or
(c) RTITADTFRKLFRVYSNFLRGKLKLYTGEACRT (SEQ ID NO: 4; residues 131-163 of SEQ ID NO: 1); --

Please replace the paragraph beginning at line 29 on page 8 of the specification with the following amended paragraph:

-- an accordingly specified molecule wherein alteration is conducted at one or more residues from the string of contiguous residues defined herein as epitope region R1 and comprising the sequence AKEAENITTGCAEHCSLNENI (SEQ ID NO: 5; residues 19-39 of SEQ ID NO: 1); --

Please replace the paragraph beginning at line 1 on page 9 of the specification with the following amended paragraph:

-- an accordingly specified molecule wherein alteration is conducted at one or more residues from the string of contiguous residues defined herein as epitope region R2 and comprising the sequence RGQALLVNSSQPWEPLQLHVD (SEQ ID NO: 6; residues 76-96 of SEQ ID NO: 1); --

Please replace the paragraph beginning at line 4 on page 9 of the specification with the following amended paragraph:

-- an accordingly specified molecule wherein alteration is conducted at one or more residues from the string of contiguous residues defined herein as epitope region R3 and comprising the sequence TFRKLFRVYSNFLRGKLKLYT (SEQ ID NO: 7; residues 137-157 of SEQ ID NO: 1); --

Please replace the paragraph beginning at line 1 on page 13 of the specification with the following amended paragraph:

-- Similarly the inclusion of control peptides for which there is expectation that the majority of PBMC donor samples will be responsive may be included in each assay plate. The influenza haemagglutinin peptide 307-309, sequence PKYVKQNTLKLA (SEQ ID NO: 8); and the *Chlamydia* HSP 60 peptide sequence KVVDQIKKISKPVQH (SEQ ID NO: 9) are particularly suitable control peptides although many other examples may be exploited. Assays should preferably also use a potent whole protein antigen such as hemocyanin from Keyhole Limpet to which all PBMC samples would be expected to exhibit an SI significantly greater than 2.0. --

Please replace Table 1 beginning after line 27 on page 14 of the specification with the following amended table:

PeptideID #	Residue *	SEQ ID NO:	Peptide Sequence
P4	10	13	RVLERYLLEAKEAEN
P7	19	16	AKEAENITTGCAEHC
P8	22	17	AENITTGCAEHCSLN
P9	25	18	ITTGCAEHCSLNENI
P10	28	19	GCAEHCSLNENITVP
P16	46	25	VNFYAWKRMEVGQQA
P26	76	35	RGQALLVNSSQPWEP
P27	79	36	ALLVNSSQPWEPLQL
P28	82	37	VNSSQPWEPLQLHVD
P32	94	41	HVDKAVSGLRSLTTL
P41	122	50	PDAASAAPLRTITAD
P44	131	53	RTITADTFRKLFRVY
P46	137	55	TFRKLFRVYSNFLRG
P47	140	56	KLFRVYSNFLRGKLK
P48	143	57	RVYSNFLRGKLKLYT
P50	149	59	LRGKLKLYTGEACRT

Please replace Table 2 on page 15 of the specification with the following amended table:

Peptide ID #	Residue #	SEQ ID NO:	Peptide Sequence	Epitope Region
P7	19	16	AKEAENITTGCAEHC	
P8	22	17	AENITTGCAEHCSLN	R1
P9	25	18	ITTGCAEHCSLNENI	
P26	76	35	RGQALLVNSSQPWEP	R2
P46	137	55	TFRKLFRVYSNFLRG	
P47	140	56	KLFRVYSNFLRGKLK	R3
P50	149	59	LRGKLKLYTGEACRT	

Please replace the paragraph beginning at line 1 on page 16 of the specification with the following amended paragraph:

-- Epitope region R1 is encompassed by peptides P7, P8 and P9 comprising the sequence AKEAENITTGCAEHCSLNENI (SEQ ID NO: 5; residues 19-39 of SEQ ID NO: 1). Epitope region R2 is encompassed by peptide P26 comprising the sequence RGQALLVNSSQPWEP (SEQ ID NO: 35). Note that for the R2 epitope, successive peptides P27 and P28 are also reactive each with one PBMC donor sample. In the case of the P27 peptide the donor is also reactive to the P26 peptide and it is likely that a single common core sequence within R2 is responsible for this stimulation. Owing to the phasing of each successive peptide in the sequence, it is possible that the same core nonamer sequence is shared ([[i.e]] i.e., is common) between either 2 or 3 adjacent peptides. The exact phasing is dependent on proximity to the N-terminus and tied to the length of the peptides and number of "new" residues scanned by each successive increment of the sequence. In the case of the R2 epitope, the C-terminal boundary of the epitope region has been set to include sequence covered by peptides P27 and P28 not least as this region is shown to contain significant MHC class II ligands in its C-terminal region (see later and FIGURE 2). Epitope region R2 is accordingly defined by the sequence RGQALLVNSSQPWEPLQLHVD (SEQ ID NO: 6; residues 76-96 of SEQ ID NO: 1). --

Please replace the paragraph beginning at line 4 on page 26 of the specification with the following amended paragraph:

-- Epitope region R3 is encompassed by peptides P46 and P47 and extends toward the C-terminus of the EPO sequence. The C-terminal boundary of eptope R3 is limited by the natural terminus of the EPO protein, notably peptide P50 is also reactive in two donor samples and these donors are the same as react with peptides P46 and P47. The core of the R3 epitope is considered to comprise the sequence TFRKLFRVYSNFLRGKLK (residues 137-154 of SEQ ID NO: 1), but an additional MHC class II ligand and known reactive peptide comprises the overlapping P50 peptide sequence LRGKLKLYTGEACRT (SEQ ID NO: 59) to give a total R3 sequence comprising TFRKLFRVYSNFLRGKLKLYT (SEQ ID NO: 7; residues 137-157 of SEQ ID NO: 1). --

Please replace the paragraph beginning at line 29 on page 22 of the specification with the following amended paragraph:

-- ~~FIGURE 1~~ FIGURE 1 is a depiction of the MHC class II ligands identified within epitope region R1 (SEQ ID NO: 5; residues 19-39 of SEQ ID NO: 1). Ligands are identified using the *in silico* system of EXAMPLE 2. In this case the binding profile of 18 human DR allotypes are displayed as columns. The ligands detected are 13-mers and residue number 1 of each 13-mer is identified by a coloured block. The intensity of the binding interaction (High, Medium or Low) for each peptide with respect to each of the 18 allotypes is indicated according to the key displayed. --

Please replace the paragraph beginning at line 3 on page 23 of the specification with the following amended paragraph:

-- ~~FIGURE 2~~ FIGURE 2 is a depiction of the MHC class II ligands identified within epitope region R2 (i.e., SEQ ID NO: 6; residues 76-96 of SEQ ID NO: 1). Ligands are identified using the *in silico* system of EXAMPLE 2. In this case the binding profile of 18 human DR allotypes are displayed as columns. The ligands detected are 13-mers and residue number 1 of each 13-mer is identified by a coloured block. The intensity of the binding interaction (High , Medium or Low) for each peptide with respect to each of the 18 allotypes is indicated according to the key displayed. --

Please replace the paragraph beginning at line 10 on page 23 of the specification with the following amended paragraph:

-- ~~FIGURE 3~~ FIGURE 3 is a depiction of the MHC class II ligands identified within epitope region R3 (i.e., SEQ ID NO: 7; residues 137-157 of SEQ ID NO: 1). Ligands are identified using the *in silico* system of EXAMPLE 2. In this case the binding profile of 18 human DR allotypes are displayed as columns. The ligands detected are 13-mers and residue number 1 of each 13-mer is identified by a coloured block. The intensity of the binding interaction (High , Medium or Low) for each peptide with respect to each of the 18 allotypes is indicated according to the key displayed. --

Please replace the paragraph beginning at line 17 on page 23 of the specification with the following amended paragraph:

-- ~~FIGURE 4~~ FIGURE 4 depicts a most preferred EPO structure (SEQ ID NO: 61) in which MHC class II ligands are eliminated by substitution within epitope regions R1, R2 and R3. --

Please replace the paragraph beginning at line 30 on page 24 of the specification with the following amended paragraph:

-- The control antigens used in this study were Flu haemagglutinin 307-319 (sequence: PKYVKQNTLKLAT; SEQ ID NO: 8); *Chlamydia* HSP 60 peptide (sequence: KVVDQIKKISKPVQH; SEQ ID NO: 9) and Keyhole Limpet hemocyanin. --

Please replace Table 3 on page 25 of the specification with the following amended table:

Peptide ID #	EPO; 15mer peptide sequence	SEQ ID NO:	Residue #
P1	APPRLICDSRVLERY	10	1
P2	RLICDSRVLERYLLE	11	4
P3	CDSRVLERYLLEAKE	12	7
P4	RVLERYLLEAKEAEN	13	10
P5	ERYLLEAKEAENITT	14	13
P6	LLEAKEAENITTGCA	15	16
P7	AKEAENITTGCAEHC	16	19
P8	AENITTGCAEHCSLN	17	22
P9	ITTGCAEHCSLNENI	18	25
P10	GCAEHCSLNENITVP	19	28
P11	EHCSLNENITVPDTK	20	31
P12	SLNENITVPDTKVNF	21	34
P13	ENITVPDTKVNFYAW	22	37
P14	TVPDTKVNFYAWKRM	23	40
P15	DTKVNFYAWKRMEVG	24	43
P16	VNFYAWKRMEVGQQA	25	46
P17	YAWKRMEVGQQAVEV	26	49
P18	KRMEVGQQAVEVWQG	27	52
P19	EVGQQAVEVWQGLAL	28	55
P20	QQAVEVWQGLALLSE	29	58
P21	VEVWQGLALLSEAVL	30	61
P22	WQGLALLSEAVLRGQ	31	64
P23	LALLSEAVLRGQALL	32	67
P24	LSEAVLRGQALLVNS	33	70
P25	AVLRGQALLVNSSQP	34	73
P26	RGQALLVNSSQPWEP	35	76
P27	ALLVNSSQPWEPLQL	36	79
P28	VNSSQPWEPLQLHVD	37	82
P29	SQPWEPLQLHVDKAV	38	85
P30	WEPLQLHVDKAVSGL	39	88
P31	LQLHVDKAVSGLRSL	40	91
P32	HVDKAVSGLRSLTTL	41	94
P33	KAVSGLRSLTTLLRA	42	97
P34	SGLRSLTTLLRALGA	43	100
P35	RSLTTLLRALGAQKE	44	103
P36	TTLLRALGAQKEAIS	45	106
P37	LRALGAQKEAISPPD	46	109
P38	LGAQKEAISPPDAAS	47	112
P39	QKEAISPPDAASAAP	48	115
P40	AISPPDAASAAPLRT	49	118
P41	PDAASAAPLRTITAD	50	122
P42	ASAAPLRTITADTFR	51	125
P43	APLRTITADTFRKLF	52	128
P44	RTITADTFRKLFRVY	53	131
P45	TADTFRKLFRVYSNF	54	134
P46	TFRKLFRVYSNFLRG	55	137
P47	KLFRVYSNFLRGKLK	56	140
P48	RVYSNFLRGKLKLYT	57	143
P49	SNFLRGKLKLYTGEA	58	146
P50	LRGKLKLYTGEACRT	59	149
P51	KLKLYTGEACRTGDR	60	152

Please replace Table 4 beginning on page 26 of the specification with the following amended table:

Peptide ID #	SEQ ID NO:	Peptide Sequence	Responsive Allotypes
P4	13	RVLERYLLEAKEAEN	DRB1*11, DRB1*0103, DRB3
P7	16	AKEAENITTGCAEHC	DRB1*04, DRB1*07, DRB4*01 DRB1*01, DRB1*08 DRB1*10, DRB1*13, DRB3
P8	17	AENITTGCAEHCSLN	DRB1*01, DRB1*08 DRB1*10, DRB1*13, DRB3 DRB1*11, DRB1*15, DRB3, DRB5
P9	18	ITTGCAEHCSLNENI	DRB1*01, DRB1*08 DRB1*10, DRB1*13, DRB3
P10	19	GCAEHCSLNENITVP	DRB1*01, DRB1*08
P16	25	VNFYAWKRMEVGQQA	DRB1*11, DRB1*0103, DRB3
P26	35	RGQALLVNSSQPWEP	DRB1*10, DRB1*13, DRB3 DRB1*11, DRB1*15, DRB3, DRB5
P27	36	ALLVNSSQPWEPLQL	DRB1*11, DRB1*15, DRB3, DRB5
P28	37	VNSSQPWEPLQLHVD	DRB1*10, DRB1*13, DRB3
P32	40	HVDKAVSGLRSLTTL	DRB1*04, DRB1*07, DRB4*01
P41	50	PDAASAAPLRTITAD	DRB1*15, DRB1*0103, DRB5
P44	53	RTITADTFRKLFRVY	DRB1*11, DRB1*0103, DRB3
P46	55	TFRKLFRVYSNFLRG	DRB1*13, DRB1*14 or DRB1*14 only, DRB3 DRB1*11, DRB1*0103, DRB3
P47	56	KLFRVYSNFLRGKLK	DRB1*13, DRB1*14 or DRB1*14 only, DRB3 DRB1*11, DRB1*0103, DRB3
P48	57	RVYSNFLRGKLKLYT	DRB1*11, DRB1*0103, DRB3
P50	59	LRGKLKLYTGEACRT	DRB1*13, DRB1*14 or DRB1*14 only, DRB3 DRB1*11, DRB1*0103, DRB3

Please replace the paragraph beginning at line 17 on page 28 of the specification with the following amended paragraph:

-- An EPO structure containing the most preferred set of substitutions according to the above scheme is depicted below (SEQ ID NO: 61) and in FIGURE 4. --